

## **REMARKS**

### **Claim of Priority**

Upon further review, Applicants find that the Examiner is correct that the earliest priority claimed in the instant application is 9/26/2000.

### **Claim Amendments**

Claim 9 has been amended to remove 2'-O-methyl from the recited immunostimulatory moieties of X4. Claim 11 has been amended herein to depend on claim 9. No new matter has been added.

### **Indefiniteness of claim 11**

Claim 11 has been amended herein to depend on claim 9. Accordingly, this rejection has been overcome by amendment.

### **Rejection of Claim 9 Under 35 U.S.C. §102(a)**

Claim 9 is rejected under 35 U.S.C. §102(a) as being anticipated by Zhao et al. However, this rejection ignores the proviso of claim 9 that at least one of X1, X2, X3, or X4 is one of the recited immunostimulatory moieties. Accordingly, Applicants respectfully submit that Schwartz et al does not anticipate claim 9 and request that this rejection be withdrawn.

### **Rejection of Claims 9 and 11 Under 35 U.S.C. §102(b)**

Claims 9 and 11 are rejected under 35 U.S.C. §102(b) as being anticipated by Ngyuen et al. Again, this rejection ignores the proviso of claim 9 that at least one of X1, X2, X3, or X4 is one of the recited immunostimulatory moieties. Accordingly, Applicants respectfully submit that Nguyen et al does not anticipate claim 9 or 11 and request that this rejection be withdrawn.

### **Rejection of Claims 9-11 and 39 Under 35 U.S.C. §103(a): Schwartz**

Claims 9-11 and 39 are rejected under 35 U.S.C. §103(a) as being unpatentable over Schwartz et al.

Applicants respectfully disagree. Claim 39, like claims 9 and 11 (discussed above), requires that at least one of X1, X2, X3, or X4 is one of the recited immunostimulatory moieties. Schwartz does not teach or suggest this limitation.

Moreover, with respect to claim 39, the current rejection over-reads the teaching of Schwartz. In particular, the current rejection asserts that “Schwartz et al discloses that non-natural purine nucleosides can be used as an alternative to the natural purine nucleosides. [Lines 22-32, page 12 in particular.]”. However, Schwartz, at page 12, lines 28-29, teaches that this is true only “as long as the other criteria of the present invention are satisfied”.

What are these other criteria? At page 10, lines 5-8, Schwartz recites as follows.

A composition of the subject invention is a modified ISS which is capable of eliciting a desired immune response upon administration. The term “modified ISS” as used herein refers to oligonucleotide sequences that effect a measurable immune response and comprise a CG dinucleotide in which the C residue is modified ...” (emphasis added)

Thus, for the “other criteria” to be satisfied, the CG dinucleotide must be present (not a modified C in combination with anything other than G). There is no exemplification anywhere in Schwartz to suggest an ISS in which both the C and G are modified, nor that such compounds would have immunostimulatory activity. A fair reading of Schwartz is that it allows incorporation of purine analogs at other locations within the sequence, so long as the compound retains the immune stimulatory CG dinucleotide (in which the C is modified) is retained.

The rejection further states that “One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the substitution of equivalents is routinely practiced in the art.” However, there is absolutely no evidence of record that, at the time the invention was made, in the art of oligonucleotide-based immune stimulatory compounds, that non-natural purine nucleosides were regarded as equivalents of guanosine in the context of an immunostimulatory CG dinucleotide. In fact, Applicants affirmatively represent that this was not the case. This discovery was made solely by Applicants and is part of Applicants’ invention. Nothing in the prior art suggested that a compound having a substitution for G in the CG dinucleotide would have immunostimulatory activity. For the Examiner’s convenience, an analysis of the relevant teachings of Schwartz is Attached as an exhibit. (This analysis uses Schwartz USPN 6,562,796 rather than WO/9962923, but the specifications are identical.)

For these reasons, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claim 39 Under 35 U.S.C. §103(a): Nguyen in view of Schwartz

Claim 39 is rejected as being obvious over Nguyen et al in view of Schwartz et al. Applicants respectfully disagree. As discussed above, neither Nguyen nor Schwartz teaches or suggests the limitation of claim 39 that “at least one of X1, X2, X3, or X4 is” one of the recited immunostimulatory moieties. As also discussed above, Schwartz does not teach or suggest the use of a non-natural purine as a substitute for guanosine in the context of the CG dinucleotide, and such substitutions were not regarded as equivalents in such a context in this art. Nguyen does nothing to remedy this deficiency. Moreover, one of ordinary skill in the art would not be motivated to combine Schwartz, in the oligonucleotide-based immunostimulatory compounds, with Nguyen, in the non-analogous art of DNA sequencing. For these reasons, Applicants respectfully request that this rejection be withdrawn.

Rejection of Claims 9, 11 and 39 Under 35 U.S.C. §103(a): Zhao in view of Schwartz

Claims 9, 11 and 39 are rejected as being obvious over Zhao et al in view of Schwartz et al. Applicants respectfully disagree. Schwartz neither teaches nor suggests the limitation of the claims that “at least one of X1, X2, X3, or X4 is” one of the recited immunostimulatory moieties. Zhao does teach an immunostimulatory oligonucleotide having an X4 that is a 2'-O-methylnucleoside (Table 1, compound 6). However, claim 9 has been amended to remove 2'-O-methyl as an immunostimulatory moiety in X4.

With respect to claim 39, and as discussed above, Schwartz does not teach or suggest the use of a non-natural purine as a substitute for guanosine in the context of the CG dinucleotide, and such substitutions were not regarded as equivalents in such a context in this art. Zhao does nothing to remedy this deficiency. For these reasons, Applicants respectfully request that this rejection be withdrawn.

Rejection of Claims 9-11 Under 35 U.S.C. §103(a)

Claims 9-11 are rejected under 35 U.S.C. §103(a) as being unpatentable over Zhao et al. in view of Schwartz et al.

Applicants respectfully disagree. As state above, Agrawal fails to teach or suggest the claimed invention. Furthermore, as discussed, Schwartz fails to provide the teachings that Agrawal lacks. Reconsideration and withdrawal of the rejection are respectfully requested.

#### Double Patenting

Claims 9-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 23 of co-pending Application No. 11/274,043.

As stated by the Examiner, this is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. Please note that U.S. Application No. 11/274,043 is the later filed application.

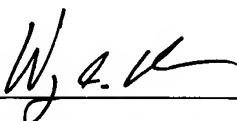
Therefore, if this provisional double patenting rejection is the only remaining rejection in the application, Applicants request that the Examiner withdraw the rejection in the instant [earlier filed] application thereby permitting this application to issue without need of a terminal disclaimer. (See MPEP §804(I)(B)). Applicants will then consider filing a Terminal Disclaimer or take any other action deemed necessary in the later filed, co-pending application.

#### CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

Dated: 6/18/08  
Keown & Zucchero, LLP  
500 West Cummings Park  
Suite 1200  
Woburn, MA 01801  
Telephone: 781/938-1805  
Facsimile: 781/938-4777

By:   
Wayne A. Keown  
Registration No. 33,923